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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/240,455	01/29/1999	DAVID D. MUNDSCHENK	15050.5	7348

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EXAMINER
WARE, TODD

ART UNIT	PAPER NUMBER
1615	20

DATE MAILED: 11/19/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/240,455	MUNDSCHENK, DAVID D.	
	Examiner	Art Unit	
	Todd D Ware	1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1 and 3-69* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1 and 3-69* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Receipt of request for extension of time (granted) and request for reconsideration both filed 9-3-02 is acknowledged. Claims 1 and 3-69 are pending.

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 9-3-02 has been entered.

Claim Rejections - 35 USC § 103

2. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

3. Claims 1, 3-4, 9-50, 52-69 are rejected under 35 U.S.C. 103(a) as being unpatentable over Mundshenk et al (WO 97/43407; hereafter '407) in combination with Heiber et al (US 5,766,620; hereafter '620) and further in combination with Siegel et al (1995).

4. '407 teaches a method of preparing inactivated toxins and bioactive peptides and methods for their administration involving inactivation of a toxin or bioactive peptide with ozone and administering the inactivated peptide parenterally as a vaccination. These peptides may be prepared by the use of ozonated water to prevent the formation of disulfide bridges. The method of '407 also uses the method of preparing a cDNA strand encoding the peptide. For toxins, see the table in column 5. For protein hormones, see the paragraph bridging columns 4 and 5. '407 does not teach buccal administration of the peptides or inclusion of a quaternary ammonium salt such as benzalkonium chloride for enhancing mucosal absorption of the peptide in the buccal cavity.

5. '620 is relied upon for teaching that peptides are buccally administratable. '620 employs adhesive tablets containing a peptide and a permeation enhancer to deliver the peptides buccally.

6. Siegel et al demonstrates that surfactants such as benzalkonium chloride increase the penetration rate of compounds across oral mucosa.

7. Accordingly, it would have been obvious to one skilled in the art at the time of the invention to combine the teachings of '407, '620, and Siegel et al to provide a non-invasive route of administration for inactivated peptides to vaccinate an individual that uses benzalkonium chloride to enhance the mucosal absorption of the composition.

8. Claims 5-8 and 51 are rejected under 35 U.S.C. 103(a) as being unpatentable over Mundshenk et al (WO 97/43407; hereafter '407) in combination

with Kamiya et al (US 4,948,588; hereafter '588) and further in combination Siegel et al (1995).

9. '407 is relied upon for all that it teaches as previously stated. '407 does not teach delivering a composition by spraying to the roof of the mouth or inclusion of a quaternary ammonium salt such as benzalkonium chloride for enhancing mucosal absorption of the peptide in the buccal cavity.

10. '588 is relied upon for teaching buccal administration of peptides by spraying compositions of peptides with absorption enhancing agents in aerosol and non-aerosol formulations.

11. Dondeti et al is relied upon for teaching that 0.02% benzalkonium chloride is effective at enhancing mucosal absorption of insulin (pages 102-103).

12. Accordingly, it would have been obvious to one skilled in the art at the time of the invention to combine the teachings of '407, '588, and Dondeti et al to provide a non-invasive route of administration for inactivated peptides to vaccinate an individual that uses benzalkonium chloride to enhance the mucosal absorption of the composition.

Response to Arguments

13. As applicant's statements are applicable to both 35 U.S.C. 103(a) rejections, the following response to arguments are based upon both rejections. Applicant's arguments filed 9-3-02 have been fully considered but they are not persuasive. Applicant argues that the peptides of '407 are unlikely to be delivered to the body, since they include a variety of toxins. This argument is not persuasive or not understood.

The peptides of '407 are designed specifically to be delivered to the body as stated in the second paragraph of the background of the invention, "it is desirable to prepare otherwise bioactive polypeptides in their inactive form, in which they can be used for other *in vivo* purposes, such as the preparation of vaccines," (page 1, lines 15-17). The last paragraph of page three to line 18 of page four furthers this concept in teaching the preparation of a parenteral composition. Accordingly, this is not found persuasive.

Applicant further argues that Siegel fails to provide any significant improvement as compared to the control as levels within applicant's most preferred ranges as shown in the specification. It is again noted that only claims 13-14 require a particular amount of benzalkonium chloride. It is resubmitted that Siegel teaches amounts within these ranges. Applicant argues that these ranges are not shown to provide a significant improvement, however the examiner disagrees. These concentrations are shown by Siegel to be significant at P values less than 0.05, 0.01, and 0.001 for test molecules. This shows that it is obvious to adjust the amount of benzalkonium chloride in accordance with the agent to be absorbed.

14. Claims 7-10 and 30-69 are rejected under 35 U.S.C. 103(a) as being unpatentable over Mundshenk et al (WO 97/43407; hereafter '407 in combination with Kamiya et al (US 4,948,588; hereafter '588) and further in combination with Cardinaux et al (US 5,578,567; hereafter '567).

15. '407 is relied upon for all that it teaches as previously stated. '407 does not teach buccal administration of the peptides or inclusion of a quaternary ammonium salt

such as benzalkonium chloride for enhancing mucosal absorption of the peptide in the buccal cavity.

16. '588 is relied upon for teaching aerosol and non-aerosol peptide formulations.

17. '567 is relied upon for teaching mucosal peptide formulations that contain benzalkonium chloride as a preservative.

18. Accordingly, it would have been obvious to one skilled in the art at the time of the invention to combine the teachings of '407, '588, and '567 to provide a non-invasive route of administration for inactivated peptides to vaccinate an individual that contains benzalkonium chloride to protect the composition against bacterial contamination. Manipulation of the amount of benzalkonium chloride to include in the formulation would be obvious to one skilled in the art in an effort to maximize the antibacterial properties of benzalkonium chloride.

Response to Arguments

19. Applicant's arguments filed 9-3-02 have been fully considered but they are not persuasive. Applicant's arguments filed 4-9-01 have also been re-evaluated in view of the composition claims. In those arguments, applicant submits that the references do not teach that the benzalkonium chloride enhances permeation of inactivated peptide and that benzalkonium chloride is included only in a laundry list of preservatives. This argument is not found persuasive. The benzalkonium chloride is only one of five elements in the list applicant submits is a laundry list. Furthermore, applicant's comments regarding inclusion of benzalkonium chloride as a preservative and not as a

permeation enhancing compound are not found persuasive, since such a limitation of a composition is an intended use process limitation and is not afforded patentable weight.

Conclusion

20. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Todd D Ware whose telephone number is (703) 305-1700. The examiner can normally be reached on 7:30 AM - 4 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Thurman K Page can be reached on (703)308-2927. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4556 for regular communications and (703) 308-4556 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-1234.

THURMAN K. PAGE
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600

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November 18, 2002